**UTILITY OF CLAIMS 1-10 and 18-37 UNDER 35 U.S.C. §101 AND §112, 1st ¶**

Claims 1-10 and 18-37 stand rejected as lacking a specific and substantially well established utility under §§ 101 and 112, first paragraph. This rejection is respectfully traversed.

The rejected claims are directed to isolated molecules comprising an antibody variable region which specifically binds to an extracellular domain of TEM17 as shown in SEQ ID NO: 230. The PTO urged that the claimed subject matter lacked a substantial utility because "the specification offers little information about the actual existence of the TEM17 protein or its functional role." Paper No. 03122004, page 3, lines 17-18.

Applicants previously urged that the PTO had not shifted the burden to applicants to warrant a showing of its asserted utility. See amendment dated August 18, 2004, at page 5. Nonetheless, in order to expedite prosecution Applicants submitted a declaration of Dr. Kenneth Kinzler ("the Kinzler Declaration") which set forth data which demonstrated that:

- TEM17 protein is expressed in tumor endothelium but not in normal endothelium;
- the extracellular domain of TEM17 protein binds to a protein known as cortactin, which is known to be involved in cell migration and the cytoskeleton;
- radiolabeled antibodies raised against TEM17 protein specifically label tumor tissues *in vivo*.

Although the Kinzler Declaration addressed the substance of the doubts which were raised regarding the utility of the present invention, the PTO nonetheless found the Kinzler Declaration unpersuasive. Paper No. 5122005. The PTO asserted that the Kinzler Declaration was insufficient to overcome the rejection because it did not reflect the state of the art ***at the time of filing*** of the application. Therefore, the PTO concluded, utilities related to the new evidence

were not realized at the time of filing by the applicants. Paper No. 5122005, page 3, line 7, and following.

Applicants did, however, realize, recognize, and teach specific and substantial utilities for the claimed antibodies ***at the time of filing*** of the application. This is demonstrated at the following paragraphs of the specification ***as filed***:

- paragraph [08] which teaches that the claimed antibodies are useful for inhibiting neoangiogenesis.
- paragraph [09] which teaches that the claimed antibodies are useful for inhibiting tumor growth.
- paragraph [22] which teaches that the claimed antibodies are useful for identifying regions of neoangiogenesis.
- paragraph [24] which teaches that the claimed antibodies are useful for detecting TEM17 in a body fluid, which indicates neoangiogenesis in the body.
- paragraph [121] which teaches that the claimed antibodies are useful for restricting, inhibiting, reducing, and/or diminishing tumor or other abnormal, undesirable, vasculature growth.

These are specific and substantial utilities which applicant clearly recognized at the time of filing.

Moreover, contrary to the position taken by the PTO (Paper No. 5122005), the courts have repeatedly held that post-filing date evidence may be provided to show the truth or accuracy of statements made in the specification. The Court of Customs and Patent Appeals explained in *In re Pottier,* that "whether or not an invention would be deemed operative by one

of ordinary skill in the art is determined, not at the time the invention was made but rather (at the earliest) at the time of the examiner's call for proof." 153 U.S.P.Q. 407, 408 (1967). Ten years later the same court laid out six situations where post-filing date publications could be used as evidence with regard to issues under Section 112. *In re Hogan,* 194 U.S.P.Q. 527, 537 (1977). Two of these situations are: a showing "that a statement in the specification was inaccurate;" and a showing "that the invention was inoperative or lacked utility." The same court explained that the PTO can use post-filing date references "to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought" because "the question would be regarding the *accuracy* of a statement in the specification, not whether that statement had been made before." *In re Marzocchi,* 169 U.S.P.Q.367, 370 (1971). The *Hogan* court further held that "[c]ourts should not treat the same legal question, enablement under § 112, in one manner with respect to the applicant and in a different manner with respect to the examiner." Because the Kinzler Declaration was provided to demonstrate the truth or accuracy of the statements of utility made in the specification as filed, and to rebut the truth or accuracy of the assertions made by the PTO in its rejection, the data contained in the declaration need not have been collected or published prior to the filing date of the application.

Moreover, MPEP §2124 entitled, "Exception to the Rule That the Critical Reference Date Must Precede the Filing Date," states: "In certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. *In re Wilson*, 311 F.2d 266, 135 USPQ 442 (CCPA 1962). Such facts include the characteristics and properties of a material or a scientific truism." The Kinzler Declaration provides facts which constitute characteristics and properties of TEM17. The Kinzler Declaration therefore should be considered fully and found persuasive.

Applicants request that the PTO reconsider the rejection in view of the evidence provided by the Kinzler Declaration. It is respectfully submitted that when all of the evidence is properly considered, including both the specification and the Kinzler Declaration, it will be clear that applicants have disclosed a specific and substantial utility for the claimed invention.

Withdrawal of these dual rejections under § 112 and § 101 is respectfully requested.

**REJECTION OF CLAIMS 26-30 UNDER §112, first paragraph**

Claims 26-30[1] are rejected as failing to comply with the written description requirement. Specifically, the post-filing date claims are said not to be supported adequately in the specification as originally filed. This rejection is respectfully traversed.

The PTO's Written Description Guidelines state that "[i]f a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met," citing *Vas-Cath Inc. v. Marhurkar,* 935 F.2d 1555 at 1563, 19 USPQ2d 1111 at 1116 (Fed. Cir. 1991); *Martin v. Johnson,* 454 F.2d 746,751, 172 USPQ 391, 395 (CCPA 1972) (stating the description need not be in *ipsis verbis* [*i.e.,* in the same words] to be sufficient.)

Claims 26-30 ultimately depend from claim 1. Claim 1 recites an "isolated molecule comprising an antibody variable region which specifically binds to an extracellular domain of TEM17." Claims 26-30 recite that the antibody specifically binds to residues 137-244 or 280-344 of TEM17.

Paragraph [07] of the specification discloses: "One embodiment of the invention provides an isolated molecule comprising an antibody variable region which specifically binds to

[1] Claim 31 contains the same recitation as claims 26-30. The discussion above applies to claim 31 as well as claims 26-30.

an extracellular domain of a TEM protein selected from the group consisting of: 1, 3, 9, 17, 19, and 44, as shown in SEQ ID NO: 196, 200, 212, 230, 232, and 271, respectively."

Paragraph [105] of the specification further discloses: "Characterization of extracellular regions for the cell surface and secreted proteins from the protein sequence is based on the prediction of signal sequence, transmembrane domains and functional domains. Antibodies are preferably specifically immunoreactive with membrane associated proteins, particularly to extracellular domains of such proteins or to secreted proteins. Such targets are readily accessible to antibodies, which typically do not have access to the interior of cells or nuclei."

Paragraph [72] of the specification discloses that the extracellular domain comprises residues 1-426 and discloses two subregions of the extracellular domain consisting of residues 137-244 and 280-344. Paragraph [72] teaches:

> TEM 17 (BSC-TEM 7) has a signal sequence which includes residues 1-18 and a transmembrane domain at residues 427-445. It is a cell surface marker with an extracellular region comprising residues 1-426. It has homologs in both mouse and *C. elegans*. Residues 137-244 share weak homology with nidogen; residues 280-344 share homology to PSI domains found in plexin, semaphorins and integrin beta subunits. Variants have been observed at nucleotides 1893(A,G), 1950(C,G), 2042(A,G), and 2220(G,A). In mouse TEM 17 the signal sequence includes residues 1-19.

(emphasis added). Thus both subregions of the extracellular domain are disclosed in the specification as originally filed. A disclosure of antibodies which bind to the extracellular domain inherently constitutes a disclosure of antibodies which bind to either of these two, large, disclosed subregions of the extracellular domain.

One of skill in the art reading the above-quoted disclosures would have understood that the inventors were in possession of the claimed invention at the time of filing, as required by the

Written Description Guidelines. Such possession need not be demonstrated by a disclosure which is in *ipsis verbis*. *Martin, supra.* Thus claims 26-30 comply with Section 112, first paragraph, and do not constitute new matter.

Withdrawal of this rejection is respectfully requested.

Respectfully submitted,

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By: Sarah A. Kagan
Sarah A. Kagan
Registration No. 32,141

Banner & Witcoff, Ltd.
Customer No. 22907